



UNITED STATES DEPARTMENT OF COMMERCE
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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
07/106,232	10/07/87	SMITH	148-120CIP3

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EXAMINER

KRUPEN, K

ART UNIT	PAPER NUMBER
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187

16

DATE MAILED:

06/19/90

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 4/16/90 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

- | | |
|---|--|
| 1. <input type="checkbox"/> Notice of References Cited by Examiner, PTO-892. | 2. <input type="checkbox"/> Notice re Patent Drawing, PTO-948. |
| 3. <input type="checkbox"/> Notice of Art Cited by Applicant, PTO-1449. | 4. <input type="checkbox"/> Notice of Informal Patent Application, Form PTO-152. |
| 5. <input type="checkbox"/> Information on How to Effect Drawing Changes, PTO-1474. | 6. <input type="checkbox"/> |

Part II SUMMARY OF ACTION

1. ☒ Claims 1-30 are pending in the application.

Of the above, claims 23-30 remain are withdrawn from consideration.

2. ☐ Claims have been cancelled.

3. ☐ Claims are allowed.

4. ☒ Claims 1-22 are rejected.

5. ☐ Claims are objected to.

6. ☐ Claims are subject to restriction or election requirement.

7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8. ☐ Formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).

10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).

12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received
☐ been filed in parent application, serial no. _____; filed on _____

13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

EXAMINER'S ACTION

Art Unit 187

The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, as the disclosure is enabling only for claims limited to the particular covalently bonded dye-fragment attachments shown to be useful, i.e., the set of 4 fluorophores with different emission spectra. See MPEP 706.03(n) and 706.03(z).

Applicants' claims are directed to colored or fluorescent labels. Applicants have disclosed on page 10 that the coupling of the tags is described in patent # 4,849,513. Applicants' claims are enabled only for such methods of coupling.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. 112, first paragraph, as failing to provide an enabling disclosure.

The invention is enabled for a selected set of four

Art Unit 187

fluorophores with different emission spectra tagged to four different nucleotides. Nothing less than 4 different fluorophore tags with 4 varying emission spectra are enabled in the DNA sequencing process set forth in the invention.

Applicants argue that the specification enables one skilled in the art to use a wide range of fluorophores having highly resolvable extinction coefficients which can be selected for by the skilled artisan for use in the instant invention. Applicants further argue that the novelty resides in the use of the fluorophores to label DNA fragments to permit their detection by automated means and therefore they should not be limited to only four fluorophores. The examiner disagrees with this argument since it appears that in order to enable the instant invention using fluorophores to sequence DNA by automated means a minimum of four fluorophores are required and nothing less more or less than 4 fluorophores with different emission spectra will permit one to detect the 4 different nucleotides by applicants, improved method of use.

Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, for the reasons set forth in the objection to the specification.

Art Unit 187

Claims 1-6 are rejected under 35 U.S.C. 103 as being unpatentable over Kaplan et al and applicants' disclosure of the methods of Maxim and Gilbert and Sanger described beginning on page 3 of the specification in view of Khanna et al.

Kaplan et al teach the separation of samples by gel electrophoresis and detection of separated material by ultraviolet transmitting material, column 3, lines 5-10. The disclosure also recites the Maxam and Gilbert and Sanger methods in which radiolabeled oligonucleotide samples are separated by gel electrophoresis for the purpose of sequencing DNA. Khanna et al disclose that fluorescent dye molecules may be attached to oligonucleotides (column 21, lines 48-51).

It would have been obvious for one skilled in the art to substitute fluorescent oligonucleotide tagged dyes as taught by Khanna et al in DNA sequencing experiments for radioactive phosphate labels as taught by Maxam and Gilbert and Sanger methods for separating DNA fragments for the purpose of utilizing non-hazardous material in the laboratory.

Applicants argue that Khanna et al disclose a class of di(chalcogen ether) symmetrically substituted fluorescein compounds which are useful when conjugate to polypeptides or solid supports for used in immunoassays and nothing disclosed is pertinent to the instant inventions of DNA sequencing. The

Art Unit 187

examiner disagrees. Khanna does in fact teach the florescent labelling of nucleotide compounds such as nucleotides and nucleosides which are the components of DNA. The DNA sequencing method is not taught by Khanna but instead by Maxam and Gilbert and Sanger. It is not taught in either reference that substitution of an non-radiocompound is favorable over radiolabeled tags but is well understood within the art that any methods that substitute radiolabels with other tags are preferred for reasons that are health related.

Claims 15-22 are allowable as they were previously.

Claims 7-14 contain allowable subject matter if the claims would be amended to include the four different emission spectra fluorescent tags.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). The practice of automatically extending the shortened statutory period an additional month upon the filing of a timely first response to a final rejection has been discontinued by the Office. See 1021 TMOG 35.

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS

Serial No. 07/106,232

-6-


Art Unit 187

OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 CFR 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication should be directed to Karen I. Krupen, Ph.D. at telephone number (703) 557-0658.

kik

5/16/90



CHRISTINE NUCKER
PRIMARY EXAMINER
ART UNIT 187